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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,945	11/10/2000	Joseph A. Sorge	25436/1190	3915

27495 7590 09/10/2002

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EXAMINER

SISSON, BRADLEY L

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 09/10/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/709,945

Applicant(s)

SORGE, JOSEPH A.

Examiner

Bradley L. Sisson

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— The MAILING DATE of this communication appears on the cover sheet with the correspondence address —

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2001 and 20 June 2002.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 November 2000 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As presently worded, the claims have sufficient breadth of scope to encompass arrays of oligonucleotides that can be of virtually any length, up to 599 nucleotides in length. The specification teaches at example 1, page 36, that an array had been manufactured, the number of different oligonucleotides synthesized, and their lengths, is not readily apparent. The aspect of one of skill in the art being able to effectively produce pure populations of oligonucleotides of lengths up to 599 nucleotides in length is critical to enabling the making and use of the claimed invention. At column 40 of Jones (US Patent 5,858,671) the inherent obstacle in synthesizing oligonucleotide arrays is disclosed. As stated therein, "that even if the constituent enzymatic steps approach 100% completion, incompletely processed products can accumulate to significant levels. For example, during oligonucleotide synthesis of a 70-mer, requiring 69 couplings, a 99% coupling efficiency results in only 50% of the generated oligonucleotides being full length ($0.99^{69} = 0.50$)."
- In the present case, applicant is claiming a product that would be the result of

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598 couplings, not just 69 as described above. Accordingly, to perform 598 couplings, with a 99% reaction completion rate, would result in only 0.2% of the product actually having the desired length.

3. At page 36 of the specification it is asserted that "[t]he human cDNA microarray [was] produced from cloned selected at random from the clone collection, as diagramed in Figure 1A. Plasmid DNA of each clone is isolated by means known in the art." At page 40 it is stated that "[t]he 3' cDNA PCR products (nucleic acid members) [were] stably associated with a substrate which is a standard 25 mm X 75 mm glass microscope slide either by an arrayer or manually...." Such teachings, however, especially in light of the art-recognized "inherent obstacle in synthesizing oligonucleotide arrays," are not sufficient to enable the production of the now claimed array. While the specification need not set forth each and every possible combination of method steps that may be utilized, the specification does need to provide sufficient detail so that the claimed method does not unfairly force the public to engage in undue experimentation. In the present case, the state of the prior art has advanced to the stage where certain problems are recognized as being endemic. The specification does not address how these art-recognized problems are to be overcome. Accordingly, the burden of enablement is unfairly shifted to that of the public. The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

" '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); see also *Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.')."

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"Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See *Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

"It is true . . . that a specification need not disclose what is well known in the art. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (Emphasis added)

For the above reasons, and in the absence of convincing evidence to the contrary, the specification has not been found to enable the making and use of the claimed device.

4. Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As presently worded, the claimed array can be comprised of nucleic acid sequences that are less than 600 bases in length and which are not present in any

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public database (claims 1 and 8). In view of an independent claim encompassing all of the limitations of any of its dependent claim, claims 1-13 have been interpreted as encompassing non-known/not publicly available sequences.

5. As set forth in claim 7, the array can comprise from 1,000 to 10,000 positions/oligonucleotides. Claims 1-6 and 8-13 place no upper limit on the number of oligonucleotides present. Upon review of the specification no description of said non-known sequences is provided. Accordingly, the specification does not reasonably suggest that applicant was in possession of said non-publicly known sequences at the time of filing. In support of this position, attention is directed to the decision of *Vas-Cath Inc. v. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 USC 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

For the above reasons, and in the absence of convincing evidence to the contrary, the specification fails to reasonably suggest that applicant was in possession, at the time of filing, an array that comprised either in its entirety, or in part, oligonucleotide sequences that are not known to the public.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. The term "primarily" in claim 4 is a relative term that renders the claim indefinite. The term "primarily" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Response to argument

8. At page 5, bridging to page 6 of the response received 31 October 2001, hereinafter the response, argument is advanced that claims 1-7 and 9-13 are not limited to, but do encompass non-known/not publicly available sequences. Attention is directed to claim 8 where it recites the limitation that at least 2% of the nucleic acid members on the array comprise sequences, which are not included within a public database. Attention is also directed to page 4 of the specification as providing a method by which one of skill in the art would be able to determine if a given nucleic acid sequence was known and in the public database or previously unknown and not listed in a public database.

9. At page 6 of the response argument is advanced that applicant has provided an adequate written description of the nucleic acids that are not publicly known as being 'a sequence not included in a public nucleic acid sequence database at the time the array was generated, either as a complete gene sequence, a partial gene sequence, a cDNA, or an expressed sequence tag (EST).'

10. The above argument has not been found to be persuasive towards the withdrawal of the rejection. It is well settled that in order to satisfy the written description requirement as it relates to nucleic acids, one needs to define the nucleic acids in terms of their structure (nucleotide

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sequence) or chemical or physical properties. In support of this position, attention is directed to the decision of *Fiers v. Sugano* 25 USPQ2d 1604-5 (CAFC, January 1993) wherein is stated:

We also reject *Fiers* argument that the existence of a workable method for preparing a DNA establishes conception of that material. Our statement in *Amgen* that conception may occur, *inter alia*, when one is able to define a chemical by its method of preparation requires that the DNA be claimed by its method of preparation. We recognize that, in addition to being claimable by structure or physical properties, a chemical material can be claimed by means of a process. A product-by-process claim normally is an after-the-fact definition, used after one has obtained a material by a particular process. Before reduction to practice, conception only of a process for making a substance, without a conception of a structural or equivalent definition of that substance, can at most constitute conception of the substance claimed as a process. Conception of a substance claimed *per se* without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties. . .

* * * *

The difficulty that would arise if we were to hold that a conception occurs when one has only an idea of a compound, defining it by its hoped-for function, is that would-be inventors would file patent applications before they had made their inventions and before they could describe them. That is not consistent with the statute or the policy behind the statute, which is to promote disclosure of inventions.

Attention is also directed to the decision of *University of California v. Eli Lilly and Co.* (CA FC, July 1997) 43 USPQ2d 1398 wherein is stated:

In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate written description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d

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1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

In the present case, the public is left with even less of a written description of the claimed nucleic acids, as it is that which is not known. It is less than clear how the public will be able to recognize the members of the genus. While applicant has articulated that one needs to practice a method so to determine if the sequence is in a public database, such speaks to a result that one may achieve if they made the invention. That is different from actually providing a description of the invention. It is further noted that if the sequence is unknown to all, the specification has not provided an adequate description of the nucleic acids such that one of skill would recognize the sequence as comprising a non-coding nucleotide sequence present in the 3'-end of an RNA transcript. This is especially true when the sequence is taken out of frame whereby it would not be coding when in the natural state but due to cleavage, a previously non-coding sequence would now be a coding sequence.

11. It is noted with particularity that claim 1 limits the nucleic acid to where it "comprises a non-coding sequence present in a 3'-end of an RNA transcript...[and] has less than 600 nucleotides." At page 6, last paragraph, of the response, however, argument is advanced that the nucleic acid member could well be "a complete gene sequence, a partial gene sequence, a cDNA, or an expressed sequence tag (EST)." Clearly, "a complete gene sequence" speaks to nucleic acids that are greater than 600 nucleotides in length. Additionally, the aspect of the unknown

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sequence being an EST also speaks to the unknown nucleic acid member being something other than a non-coding 3'terminus of RNA. It is not clear from applicant's argument if they are trying to broaden the scope of the claims or whether they are simply arguing limitations not present in the claims.

12. The above arguments have been fully considered and have not been found to be persuasive towards the withdrawal of the rejection.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

14. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

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16. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

17. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
September 4, 2002